

31. (Amended) The peptide analogue of claim 30, wherein the N-terminal or the C-terminal amino acid is a D-amino acid.

45. (Amended) A peptide analogue comprising at least seven amino acids selected from residues 86 to 99 of human myeline basic protein as recited in SEQ ID NO:3, including residue 91, wherein the L-lysine at position 91 is altered to another amino acid.

Please add the following new claims:

73. (NEW) A peptide analogue comprising at least seven consecutive amino acids selected from residues 86-99 of human myelin basic protein as recited in SEQ ID NO:3, including residue 91, wherein the L-lysine at position 91 is altered to another amino acid, and further comprising altering one to three additional residues selected from residues 86-90, 92-96, 98 and 99 to another amino acid.

74. (NEW) A composition comprising a peptide analogue according to any one of claims 30, 45, and 73 in combination with a physiologically acceptable carrier or diluent.

#### REMARKS

Claims 30-34, 45, 46, 48-50, 73 and 74 are now pending. Claims 1-29, 35-44, 47, and 51-72 have been canceled without prejudice to filing a continuation or divisional application thereon. Claims 30, 31, and 45 have been amended to clarify language and or to add additional sequence identifiers. Claims 72 and 73 have been added. Claims 72 finds support throughout the application including original claim 47. Support for claim 73 can be found throughout the specification as filed, as well as within claim 56. The enclosed electronic and paper copies of the Sequence Listing include no new matter that goes beyond the original application as filed, but are supplied as requested in the Notice to File Missing

goes beyond the original application as filed. Applicants respectfully submit that the above

identified application is now in compliance with 37 C.F.R. §§ 1.821-1.825 and WIPO Standard ST. 25. Accordingly, no new matter has been introduced.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with Markings to Show Changes Made".

In view of the above amendments and remarks, Applicants believe that the subject application is in condition for allowance. If the Examiner believes that there is any reason the subject application should not pass to allowance, the Examiner is encouraged to contact the undersigned at (206) 622-4900.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC



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Enclosures:

Postcard  
Paper Copy of Sequence Listing (3 pages)  
Computer Diskette  
Declaration Regarding Sequence Listing

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# **VERSION WITH MARKINGS TO SHOW CHANGES MADE**

Please amend the application as follows:

## In the Specification:

Please insert the enclosed "Sequence Listing" immediately after the section of the specification entitled "Abstract of the Disclosure" on page 30.

Please replace the paragraph beginning at page 2, line 35, with the following rewritten paragraph:

The present invention provides peptide analogues comprising at least 7 amino acids selected from residues 86 to 99 of human myelin basic protein (SEQ ID NO:3) in which either L-lysine at position 91, L-threonine at position 95, or L-arginine at position 97 is altered to another amino acid. In one embodiment, L-lysine at position 91 is altered and one to three additional L-amino acids selected from residues 86, 87, 88, 95, 98 or 99 are altered to another amino acid. In a second embodiment, L-threonine at position 95 is altered and one to three additional amino acids selected from residues 86, 87, 88, 91, 98 and 99 or 86, 87, 88, 97, 98, and 99 are altered to another amino acid. In a third related embodiment, L-arginine at position 97 is altered and one to three additional amino acids selected from residues 86, 87, 88, 95, 98 or 99 are altered to another amino acid. The peptide analogues preferably contain double or triple alterations. In preferred aspects of the invention, the peptide analogues have altered residues 91, 95 or 97 to alanine and the additional amino acids are altered to the corresponding D-form amino acid.

Please replace the paragraph beginning at page 3, line 12, with the following rewritten

selected from residues 86 to 99 of human myelin basic protein (SEQ ID NO:3) in which either L-lysine at position 91, L-threonine at position 95, or L-arginine at position 97 is altered to another amino acid, and in addition the N-terminal and C-terminal amino acids are

altered in order to reduce proteolysis upon administration of the peptide analogue. In a preferred aspect, the N- and C-terminal amino acids are of the D-form.

Please replace the paragraph beginning at page 3, line 18, with the following rewritten paragraph:

In other embodiments, the peptide analogues comprise at least seven amino acids selected from residues 86 to 99 of human myelin basic protein (SEQ ID NO:3) in which either L-lysine at position 91, L-threonine at position 95, or L-arginine at position 97 is altered to another amino acid and in addition up to three other amino acid alterations are made. Any residue within 86-99 may be altered except that in a peptide analogue in which residue 91 is altered, residue 97 may not be altered. Likewise, in a peptide analogue in which residue 97 is altered, residue 91 may not be altered.

Please replace the paragraph beginning at page 3, line 25, with the following rewritten paragraph:

Other embodiments provide peptide analogues comprising at least seven amino acids selected from residues 86 to 99 of human myelin basic protein (SEQ ID NO:3) in which either L-lysine at position 91, L-threonine at position 95, or L-arginine at position 97 is altered to another amino acid. In preferred aspects, residue 91, 95 or 97 are altered to either alanine or the corresponding D-amino acid.

Please replace the paragraph beginning at page 3, line 34, with the following rewritten paragraph:

Further aspects of the present invention provide methods of treating multiple sclerosis by administering to a patient a therapeutically effective amount of a pharmaceutical composition comprising a peptide analogue comprising at least seven amino acids selected from residues 86 to 99 of human myelin basic protein (SEQ ID NO:3) in which residues 91, 95 or 97 are altered to another amino acid. Additionally, one to three additional amino acids may be altered or the N- and C-ends are altered to reduce proteolysis upon administration.

(SEQ ID NO:2) for human myelin basic protein.

Please replace the paragraph beginning at page 5, line 28, with the following rewritten paragraph:

"Human myelin basic protein" ("MBP") refers to a protein found in the cytoplasm of human oligodendroglial cells. The nucleotide sequence and predicted amino acid sequence of human MBP are presented in Figure 1 (SEQ ID NOS: 1-2). Although not depicted in Figure 1, different molecular forms of human myelin basic protein generated by differential splicing or post-translational modification are also within the scope of this invention.

Please replace the paragraph beginning at page 6, line 18, with the following rewritten paragraph:

As noted above, the present invention provides peptide analogues comprising at least 7 amino acids selected from residues 86-99 of human myelin basic protein (SEQ ID NO:3) and including an alteration of the naturally occurring L-lysine at position 91, L-threonine at position 95, or L-arginine at position 97, to another amino acid. In one aspect, the peptide analogue includes additional alteration of one to three L-amino acids at positions 86, 87, 88, 91, 95, 97, 98 and/or 99 of human myelin basic protein as long as 91 and 97 are not both altered in the same peptide analogue. In another aspect, the peptide analogue additionally has the N-terminal and C-terminal residues altered to an amino acid such that proteolysis is reduced upon administration to a patient compared to a peptide analogue without these additional alterations. In a further aspect, the peptide analogue of MBP comprises at least seven amino acids selected from residues 86-99 (SEQ ID NO:3) and has one of the residues at position 91, 95 or 97 altered to an amino acid not present in native MBP protein. In addition to such single alterations, one to three additional alterations of residues 86 to 99 may be made, as long as residues 91 and 97 are not altered in the same peptide analogue.

Please replace the paragraph beginning at page 8, line 27, with the following rewritten paragraph:

Peptide analogues within the present invention should (a) compete for the binding of MBP (87-99) (residues 87 to 99 of SEQ ID NO:2) to MHC; (b) not cause proliferation of an MBP (87-99)-reactive T cell line; and (c) inhibit induction of experimental

In the Claims:

Please cancel claims 1-29, 35-44, 47, and 51-72, without prejudice.

Please amend the claims as follows:

30. (Amended) A peptide analogue comprising at least seven consecutive amino acids selected from residues 86 to 99 of human myelin basic protein as recited in SEQ ID NO:3, including residue 91, wherein the L-lysine at position 91 is altered to another amino acid, and the N-terminal amino acid [and] and/or the C-terminal amino acid are altered to another amino acid, such that upon administration of the peptide analogue *in vivo* proteolysis is reduced.

31. (Amended) The peptide analogue of claim 30, wherein the N-terminal [and] or the C-terminal amino acid is a D-amino acid [acids are D-amino acids].

45. (Amended) A peptide analogue comprising at least seven amino acids selected from residues 86 to 99 of human myeline basic protein as recited in SEQ ID NO:3, including residue 91, wherein the L-lysine at position 91 is altered to another amino acid.

Please add the following new claims:

73. (NEW) A peptide analogue comprising at least seven consecutive amino acids selected from residues 86-99 of human myelin basic protein as recited in SEQ ID NO:3, including residue 91, wherein the L-lysine at position 91 is altered to another amino acid, and further comprising altering one to three additional residues selected from residues 86-90, 92-96, 98 and 99 to another amino acid.

claims 1-29, 35-44, 47, and 51-72, and 73, are intended to be with a physiologically acceptable carrier or diluent.